510(k) Summary

LIPOSCIENCE

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A. 510(k) Number: K113830

B. Submitter Contact Information:

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C. Device Name:

Trade Name: Vantera® Clinical Analyzer
Common Name: *NMR LipoProfile®* test on Vantera® Clinical Analyzer
Classification Names:

Instrumentation for clinical multiplex test system, 21 CFR 862.2570, Product Code NSU
Lipoprotein test system, 21 CFR 862.1475, Product Code MRR and LBS
Cholesterol test system 21 CFR 862.1175, Product Code LBS
Triglyceride test system, 21 CFR 862.1705, Product Code CDT

Panel: Clinical Chemistry (75)

D. Legally Marketed Device to which Equivalence is Claimed (Predicate Device):

NMR Profiler and *NMR Lipoprofile* test	k111516
Luminex LX 100/200 Instrument	k073506

E. Device Description:

For the Instrument

The Vantera Clinical Analyzer is a clinical laboratory analyzer that employs nuclear magnetic resonance spectroscopic detection to quantify multiple analytes in biological fluid specimens, specifically blood plasma and serum.

The Vantera Clinical Analyzer system design is divided into 3 major subassemblies: a sample handling assembly, an NMR subassembly, and an enclosure. The Vantera Clinical Analyzer control system is distributed across three separate computers:

- The Host (1U) controls user interface, data handling, results calculation, system startup and shutdown.
- The Process Control (4U) schedules and manages all activities required to process a sample, controls all hardware in the sample handling subsystem, and manages remote access to the system.
- The NMR Control Computer controls all magnet operations.

  Two of these computers are contained within the Sample Handling Subassembly (1U and 4U) and one in the NMR Subassembly (NMR Console).

For the Assay

The *NMR LipoProfile* test involves measurement of the 400 MHz proton NMR spectrum of a plasma/serum sample, deconvolution of the composite signal at approximately 0.8 ppm to produce signal amplitudes of the lipoprotein subclasses that contribute to the composite plasma/serum signal, and conversion of these subclass signal amplitudes to lipoprotein subclass concentrations. The ~0.8 ppm plasma NMR signal arises from the methyl group protons of the lipids carried in the LDL, HDL and VLDL subclasses of varying diameters. The NMR signals from the various lipoprotein subclasses have unique and distinctive frequencies and lineshapes, each of which is accounted for in the deconvolution analysis model. Each subclass signal amplitude is proportional to the number of subclass particles emitting the signal, which enables subclass particle concentrations to be calculated from the subclass signal amplitudes derived from the spectral deconvolution analysis. LDL subclass particle concentrations, in units of nanomoles of particles per liter (nmol/L), are summed to give the reported total LDL particle concentration (LDL-P). By employing conversion factors assuming that the various lipoprotein subclass particles have cholesterol and triglyceride contents characteristic of normolipidemic individuals, HDL cholesterol and triglyceride concentrations are also derived.

F. Indications for Use

For the Instrument

The Vantera Clinical Analyzer is an automated laboratory test analyzer which measures the 400 MHz proton nuclear magnetic resonance (NMR) spectrum of clinical samples to produce signal amplitudes, converting these signal amplitudes to analyte concentration. The device includes a 400 MHz NMR spectrometer and software to analyze digitized

spectral data. This instrumentation is intended to be used with NMR based assays to detect multiple analytes from clinical samples by technologists trained in laboratory techniques, procedures and on the use of the analyzer.

For the Assay
The *NMR LipoProfile*test, when used with the Vantera Clinical Analyzer, an automated NMR spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in human serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of HDL-C and triglycerides are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease.

G. Technological Characteristics and Substantial Equivalence:

The Vantera Clinical Analyzer is as safe and effective as the predicate device, k073506. The Vantera has similar intended use and indication for use as well as the same multi-analyte capability and the same system calibration requirement as the predicate device. The minor technological differences between the Vantera and the predicate device raise no new issues of safety or effectiveness.

Instrument Comparison Table

	Luminex LX 100/200 Instrument **(Predicate)**	***Vantera Clinical Analyzer*** **(Proposed Device)**
510(k) Number	k073506	Pending
Intended Use / Indications for Use	The Luminex LX 100/200 Instrument is a clinical multiplex test system intended to measure and sort multiple signals generated in an *In Vitro* diagnostic assay from a clinical sample. This instrumentation is used with a specific assay to measure multiple similar analytes that establish a single indicator to aid in diagnosis. The device includes a signal reader unit, raw data storage mechanisms, data acquisition software and software to process detected signals.	similar
Technology	Bead based multiplexing	Nuclear magnetic resonance
Multi-Analyte	Yes	same
Detection Method	Fluorescent	400 MHz proton NMR Spectrum
System Fluidics	Utilizes system fluidics to deliver sample to the site of sample analysis	same
Specimen Sampling and Handling	Samples are manually prepared then presented to system.	Serum/Plasma Samples are diluted onboard system
System Calibration	System calibration required	same

	***Luminex LX 100/200 Instrument* (Predicate)**	***Vantera Clinical Analyzer* (Proposed Device)**
Quality Control Checks	System level quality control checks available e.g. Classification (CON1) and reporter (CON2)	similar E.g. Signal to noise ratio – internal system check that occur during system calibration
Specimen Identification	Barcode reader entry of sample ID	same
Data Acquisition Software	Posses data acquisition software and software to process detected signals	same

Similarity to the Predicate Device (Assay)

Performance data further demonstrate that the Vantera Clinical Analyzer when used with the *NMR LipoProfile* test is as safe and effective as its predicate device, k111516. As with the predicate test, the NMR LipoProfile test on Vantera is intended for the separation and quantification of LDL-P, HDL-C and triglycerides in serum and plasma, measurements of which are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease.

Assay General Attributes

	***LipoScience NMR LipoProfile®* test and NMR Profiler (Predicate)**	**Vantera® Clinical Analyzer for use with *NMR LipoProfile®* test (Proposed Device)**
510(k) Number	k111516	Pending
Intended Use / Indications for Use	The NMR LipoProfile® test, used with the NMR Profiler, an automated nuclear magnetic resonance (NMR) spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in serum and plasma using NMR spectroscopy. LDL-P and these NMR-derived concentrations of triglycerides and HDL-C are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test is performed and provided as a service by LipoScience Laboratory.	similar
Patient Population	General	same
Instrument Platform	NMR Profiler	Vantera Clinical Analyzer
Specimen	Human serum and plasma	same
Analyzer	400 MHz NMR Spectrometer	same

	***LipoScience NMR LipoProfile®* test and NMR Profiler (Predicate)**	**Vantera® Clinical Analyzer for use with *NMR LipoProfile®* test (Proposed Device)**
Reagents and Materials	• NMR Diluent 1 - aqueous solution containing Na_2EDTA (5.0mM), $CaCl_2$ (1.0mM), KCL(120mM), Na_2HPO_4-$7H_20$(50mM), (50mM), pH 7.4, 6.0 M NaOH, 1.0 M HCl. • NMR WASH - Triton X-100- 0.1%v/v, Liqui Nox 0.1% v/v in Type 2 water, pH 10.0, sodium bicarbonate (anhydrous), sodium carbonate (anhydrous), 6.0 M NaOH • NMR Calibrator - aqueous solution of Trimethyl Acetate (TMA) disodium salt (15.0 mM) containing Na_2EDTA (5.0 mM), CaC_2 (3.0 mM), KCl (120 nM), D_2O 10% v/v • NMR LipoProfile Quality Control materials 1 and 2 contains two levels of pooled human serum-based control material, labeled Control 1 and Control 2, with pre-determined target ranges, containing sodium azide as a preservative.	Similar

	***LipoScience NMR LipoProfile®* test and NMR Profiler (Predicate)**	**Vantera® Clinical Analyzer for use with *NMR LipoProfile®* test (Proposed Device)**
Spectral Deconvolution Computational Process	Linear least-squares with singular value decomposition of the spectra from each specimen.	Same
Reference Range	Distribution of LDL-P Observed in Reference population – MESA	Distribution of LDL-P observed in a general apparently healthy population of men and women

We performed analytical validations to demonstrate that the *NMR LipoProfile®* test on the Vantera Clinical Analyzer is equivalent to the *NMR LipoProfile®* test on the NMR Profiler. The comparative analytical performance is found in tables below.

Analytical Performance for LDL-P

LDL-P (nmol/L)	**Vantera clinical analyzer for use with the *NMR LipoProfile* test**			**Predicate Device k111516**		
LoB	0			0		
LoD	40.7			41		
LoQ	132			157		
Measuring Range	300-3500 nmol/L			300-3500 nmol/L		
Linearity Regression	y=1.02x+7.82			y=0.99x-22.37		
Linearity R^2	0.9949			0.9979		
Within-Run Precision	**Level 1**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
Mean	842.6	1309.5	1837.7	908	1493	1967
SD	48.5	39.1	50.3	45.4	64.8	72.8
CV%	5.8%	3.0%	2.7%	5.0%	4.3%	3.7%
Within-Lab Precision	**Level 1**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
Mean	988.6	1266.7	1943.5	920.4	1508.3	1991.8
SD	48.84	32.57	63.42	70.5	67.7	84.6
CV%	5.3%	4.0%	3.9%	7.6%	4.5%	4.3%
Method Comparison	Linear regression: y=1.03x-36.60, R=0.978			Linearity Regression: y=0.98x+45.2, R=0.973		
Medical Decision Limits	No change.			1000, 1300 and 1600 nmol/L		
Interference Study	7 Endogenous and 23 Exogenous were tested. Salicyclic acid at ≥ 1.3mmol/L was determined to interfere with LDL-P and Clopidogrel hydrogensulfate at ≥ 95.7 µmol/L was determined to interfere with LDL-P			5 Endogenous and 22 Exogenous were tested, no interference was found.		
Specimen Stability	Lipotube: Refrigerated Stability: 6 days			Lipotube: Refrigerated Stability: 5 days		

Triglycerides Analytical Performance Summary

TG (mg/dL)	Vantera clinical analyzer for use with the *NMR LipoProfile* test			Predicate Device k111516		
LoB	1.1			1.4		
LoD	2.4			2.6		
LoQ	4			2.6		
Measuring Range	5			1100		
Linearity Regression	y=1.008x-0.3979			y=0.95x-12.21		
Linearity R^2	0.9999			0.999		
Within-Run Precision	**Level 1**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
Mean	70.1	169.2	356.1	81.0	140.6	649.5
SD	1.6	3.5	4.2	2.1	2.5	8.7
CV%	2.3%	2.1%	1.2%	2.6%	1.8%	1.3%
Within-Lab Precision	**Level 1**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
Mean	68.8	166.3	352.2	78.4	145.4	624.6
SD	1.59	3.92	9.36	2.8	3.7	15.4
CV%	2.3%	2.4%	2.7%	3.6%	2.6%	2.5%
Method Comparison	Linear regression: y=1.00x+0.92, R=0.998			Linear regression: y=1.00x+1.25, R=1.00		
Medical Decision Limits	No change.			Normal (<150) Borderline-High (150-199) High (200-499) Very High (≥500)		
Interference Study	7 Endogenous and 23 Exogenous were tested, no interference was found.			5 Endogenous and 22 Exogenous were tested, no interference was found except Ibuprofen may interfere with TG measurement at and above 210µg/mL.		
Specimen Stability	Lipotube: Refrigerated Stability: 6 days			Lipotube: Refrigerated Stability: 10 days		

HDL-C Analytical Performance Summary

HDL-C (mg/dL)	**Vantera clinical analyzer for use with the *NMR LipoProfile* test**			**Predicate Device k111516**		
LoB	2.7			4.3		
LoD	3.5			5.2		
LoQ	4			5.2		
Measuring Range	7-140			7-140		
Linearity Regression	y=1.049x-0.3459			y=1.004x-0.5956		
Linearity R^2	0.9961			0.9998		
Within-Run Precision	**Level 1**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
Mean	29.1	51.1	86.9	23.7	54.9	95.1
SD	1.17	1.43	2.29	0.5	1.0	0.9
CV%	4.0%	2.8%	2.6%	2.0%	1.9%	0.9%
Within-Lab Precision	**Level 1**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
Mean	28.9	50.7	85.2	23.7	56.7	96.1
SD	0.80	1.02	1.51	0.8	1.1	1.7
CV%	2.8%	2.0%	1.8%	3.3%	2.0%	1.8%
Method Comparison	Linear regression: y=1.04x-1.20, R=0.989			Linear regression: y=1.00x+0.03, R=0.999		
Medical Decision Limits	No change.			Low(<40), High(≥60)		
Interference Study	7 Endogenous and 23 Exogenous were tested, no interference was found.			5 Endogenous and 22 Exogenous were tested, no interference was found.		
Specimen Stability	Lipotube: Refrigerated Stability: 6 days			Lipotube: Refrigerated Stability: 10 days		

H. Performance Data – Non-Clinical:

Analytical Sensitivity

The analytical sensitivity of the *NMR LipoProfile* test measurements of LDL-P, HDL-C, and triglycerides was determined as the lowest concentration measurable with acceptable precision and accuracy. Limits of quantification (LoQ), Limit of Blank (LoB) and Limit of Detection (LoD) for LDL-P, HDL-C and Triglycerides following EP17-A are listed

LDL-P
Five serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Quantification (LoQ) was mathematically calculated for LDL-P by plotting the %CV on the Y-axis against low concentration pools and determined to be: LoQ = 132 nmol/L.
Non-lipoprotein specimens were analyzed 60 consecutive times for 3 days. The Limit of Blank (LoB) was calculated non-parametrically for LDL-P and determined to be: LoB = 0.0 nmol/L.
Five serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Detection (LoD) was calculated parametrically for LDL-P and determined to be: LoD = 40.7 nmol/L.

HDL-C
Five serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Quantification (LoQ) was mathematically calculated for HDL-C by plotting the %CV on the Y-axis against low concentration pools and determined to be: LoQ = 4 mg/dL.
Non-lipoprotein specimens were analyzed 60 consecutive times for 3 days. The Limit of Blank (LoB) was calculated non-parametrically for HDL-C and determined to be: LoB = 2.7 mg/dL.
Five serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Detection (LoD) was calculated parametrically for HDL-C and determined to be: LoD = 3.5 mg/dL.

Triglycerides
Five serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Quantification (LoQ) was mathematically calculated for Triglycerides by plotting the %CV on the Y-axis against low concentration pools and determined to be: LoQ = 4 mg/dL.
Non-lipoprotein specimens were analyzed 60 consecutive times for 3 days. The Limit of Blank (LoB) was calculated non-parametrically for Triglycerides and determined to be: LoB = 1.1 mg/dL.
Five serum pools containing very low concentration were tested in replicates of 4 for 3 days. The Limit of Detection (LoD) was calculated parametrically for Triglycerides and determined to be: LoD = 2.4 mg/dL.

Assay Precision

Within-run precision and within-laboratory precision were determined by testing 20 replicates of three patient serum pools in the same run and in 20 different runs over 20 days. The pools were analyzed according to EP-5A. The results of this testing are summarized below:

Within-run Precision (n=20)

	Pool #1			Pool #2			Pool #3		
	Mean	**SD**	**%CV**	**Mean**	**SD**	**%CV**	**Mean**	**SD**	**%CV**
LDL-P, nmol/L	842.6	48.5	5.8	1309.5	39.1	3.0	1837.7	50.3	2.7
HDL-C, mg/dL	29.1	1.17	4.0	51.1	1.43	2.8	86.9	2.29	2.6
Triglycerides, mg/dL	70.1	1.6	2.3	169.2	3.5	2.1	356.1	4.2	1.2

Within-Laboratory Precision (n=80)

	Pool #1			Pool #2			Pool #3		
	Mean	**SD**	**%CV**	**Mean**	**SD**	**%CV**	**Mean**	**SD**	**%CV**
LDL-P, nmol/L	988.6	52.20	5.3	1266.7	50.08	4.0	1943.5	75.11	3.9
HDL-C, mg/dL	28.9	0.80	2.8	50.7	1.02	2.0	85.2	1.51	1.8
Triglycerides, mg/dL	68.8	1.59	2.3	166.3	3.92	2.4	352.2	9.36	2.7

Reproducibility

A reproducibility study was conducted in accordance to EP5-A2 at 3 sites incorporating five levels of serum panels at or around the medical decision limits. The panels were tested for 5 days, 6 runs per day, 2 replicates per run. The overall precision estimates are described below.

	LDL-P (nmol/L)				
Pool #	**1**	**11**	**7**	**3**	**9**
NMR 8001	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (nmol/L)	513.4	1129.4	1361.6	1957.7	3286.5
n	60	60	60	59	60
SD (nmol/L)	32.86	65.60	87.36	103.55	197.94
CV (%)	6.4	5.8	6.4	5.3	6.0
min (nmol/L)	431	988	1163	1641	2938
max (nmol/L)	573	1318	1510	2179	3636
median (nmol/L)	517	1127	1380.5	1962	3288.5
NMR 8002	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (nmol/L)	566.7	1260.6	1364.5	2050.7	3204.7
n	59	60	59	59	60
SD (nmol/L)	39.22	38.00	76.99	65.41	85.41
CV (%)	6.9	3.0	5.6	3.2	2.7
min (nmol/L)	457	1168	1155	1843	3036
max (nmol/L)	660	1346	1555	2176	3419
median (nmol/L)	574	1258.5	1366	2050	3197
NMR 8003	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (nmol/L)	479.8	1156.3	1304.4	1980.6	3153.3
n	58	60	60	60	60
SD (nmol/L)	45.00	70.60	113.21	91.78	165.47
CV (%)	9.4	6.1	8.7	4.6	5.2
min (nmol/L)	388	871	891	1671	2561
max (nmol/L)	558	1255	1491	2136	3386
median (nmol/L)	485.5	1167	1337	1999	3192
All	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (nmol/L)	520.2	1182.1	1343.4	1996.2	3214.8
n	177	180	179	178	180
SD (nmol/L)	52.94	82.19	97.37	96.39	165.44
95% CI (nmol/L)	47.94- 59.11	74.48-91.68	88.22- 108.66	87.31- 107.59	149.93- 184.55
CV (%)	10.2	7.0	7.2	4.8	5.1
min (nmol/L)	388	871	891	1641	2561
max (nmol/L)	660	1346	1555	2179	3636
median (nmol/L)	491	1165	1330	2006	3179

	HDL-C (mg/dL)				
Pool #	**1**	**8**	**4**	**10**	**11**
NMR 8001	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	21.5	33.4	53.7	80.1	92.1
n	60	60	60	60	60
SD (mg/dL)	0.75	1.39	1.81	3.70	2.61
CV (%)	3.5	4.2	3.4	4.6	2.8
min (mg/dL)	20	30	49	74	87
max (mg/dL)	23	36	57	88	97
median (mg/dL)	21.5	34	54	78.5	92
NMR 8002	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	19.4	29.2	52.3	72.9	87.5
n	59	60	60	60	60
SD (mg/dL)	0.68	1.13	1.34	1.49	1.28
CV (%)	3.5	3.9	2.6	2.0	1.5
min (mg/dL)	17	27	48	70	85
max (mg/dL)	21	31	56	76	90
median (mg/dL)	19	29	52	73	88
NMR 8003	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	19.4	28.3	49.9	74.4	84.9
n	58	60	60	60	60
SD (mg/dL)	0.90	1.41	2.36	4.26	3.39
CV (%)	4.6	5.0	4.7	5.7	4.0
min (mg/dL)	17	24	41	66	72
max (mg/dL)	21	31	53	83	89
median (mg/dL)	19	28	50	73	86
All	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	20.1	30.3	52.0	75.8	88.2
n	177	180	180	180	180
SD (mg/dL)	1.26	2.60	2.45	4.56	3.91
95% CI (mg/dL)	1.14- 1.41	2.35- 2.90	2.22- 2.73	4.14- 5.09	3.55- 4.36
CV (%)	6.3	8.6	4.7	6.0	4.4
min (mg/dL)	17	24	41	66	72
max (mg/dL)	23	36	57	88	97
median (mg/dL)	19	28	50	73	86

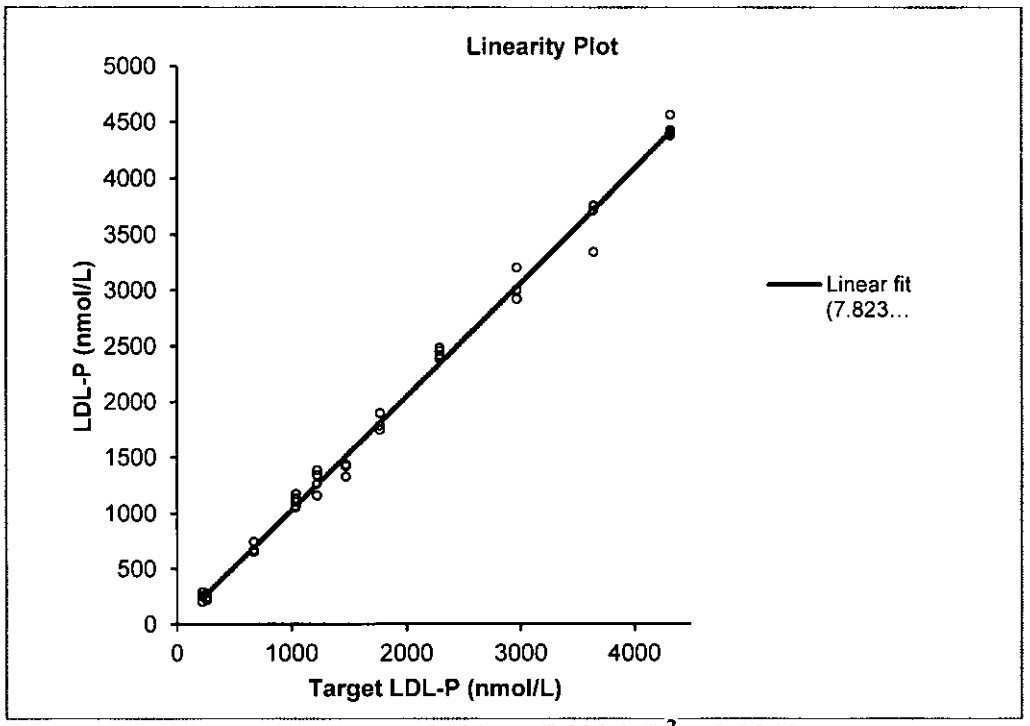
	TG (mg/dL)				
Pool #	**2**	**4**	**3**	**6**	**9**
NMR 8001	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	66.1	70.3	133.5	153.5	343.3
n	60	60	59	60	60
SD (mg/dL)	1.84	2.15	4.35	5.92	7.09
CV (%)	2.8	3.1	3.3	3.9	2.1
min (mg/dL)	61	64	120	129	321
max (mg/dL)	69	73	141	163	356
median (mg/dL)	66	71	134	155	345
NMR 8002	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	70.3	74.6	141.4	169.7	361.1
n	59	60	59	60	60
SD (mg/dL)	1.30	1.59	3.03	3.10	5.01
CV (%)	1.8	2.1	2.1	1.8	1.4
min (mg/dL)	68	72	131	160	341
max (mg/dL)	74	82	149	176	372
median (mg/dL)	70	74	142	170	361
NMR 8003	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	66.5	70.4	134.3	160.9	339.8
n	60	60	60	60	60
SD (mg/dL)	2.70	3.44	4.77	7.10	18.50
CV (%)	4.1	4.9	3.5	4.4	5.4
min (mg/dL)	57	58	119	123	267
max (mg/dL)	71	74	145	169	357
median (mg/dL)	67	72	135	162	346
All	**Panel 1**	**Panel 2**	**Panel 3**	**Panel 4**	**Panel 5**
Mean (mg/dL)	67.6	71.8	136.4	161.4	348.0
n	179	180	178	180	180
SD (mg/dL)	2.76	3.21	5.41	8.66	14.99
95% CI (mg/dL)	2.50-3.08	2.91- 3.59	4.90- 6.03	7.75- 9.66	13.59- 16.72
CV (%)	4.1	4.5	4.0	5.4	4.3
min (mg/dL)	57	58	119	123	267
max (mg/dL)	74	82	149	176	372
median (mg/dL)	67	71	135	162	344

Linearity

Three serum pools were prepared from patient specimens with low, medium and high values of LDL-P, HDL-C and Triglycerides as determined by *NMR LipoProfile* test. Each were mixed and diluted in different proportions to produce eleven (for LDL-P) or Twelve (12) (TG and HDL-C) different samples with widely varying target concentrations. Mean values from analysis of four replicates of each pool were compared to the expected target values to determine the percent bias for each sample. The serum pools were analyzed according to EP6-A. Tables and regression plots of the linearity data for LDL-P, HDL-P and Triglycerides are given below:

LDL-P Measuring Range: 300-3500 nmol/L

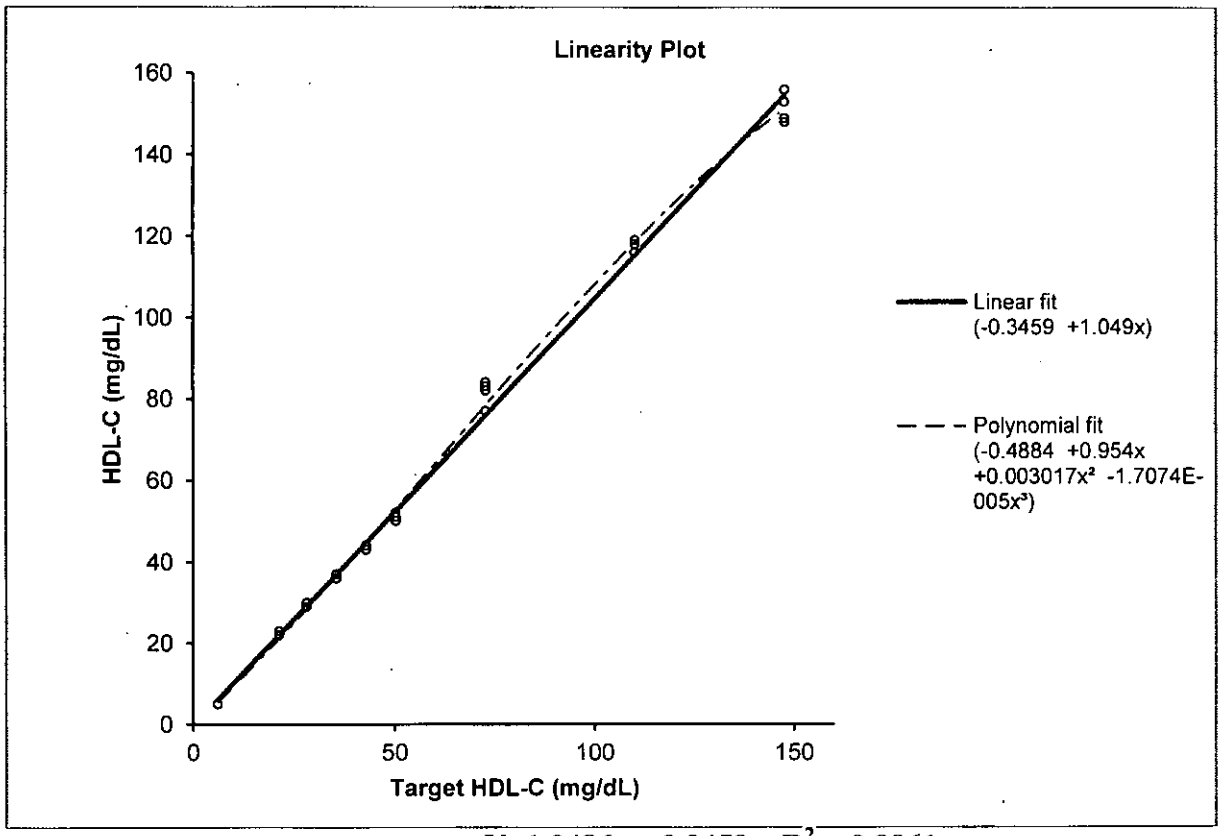
Level	1	2	3	4	5	6	7	8	9	10	11
Target value	225.4	263.375	673.75	1039.25	1222	1473.28	1770.25	2291.41	2968.22	3645.03	4321.84
Observed Mean	248.8	243.8	682.0	1115.0	1285.8	1402.3	1829.8	2437.5	3032.3	3644.3	4442.8
% Bias	10.3	-7.5	1.2	7.3	5.2	-4.8	3.4	6.4	2.2	0.0	2.8



Y=1.0193x + 7.8226, R^2 = 0.9949

HDL-C Measuring Range: 7-140 mg/dL

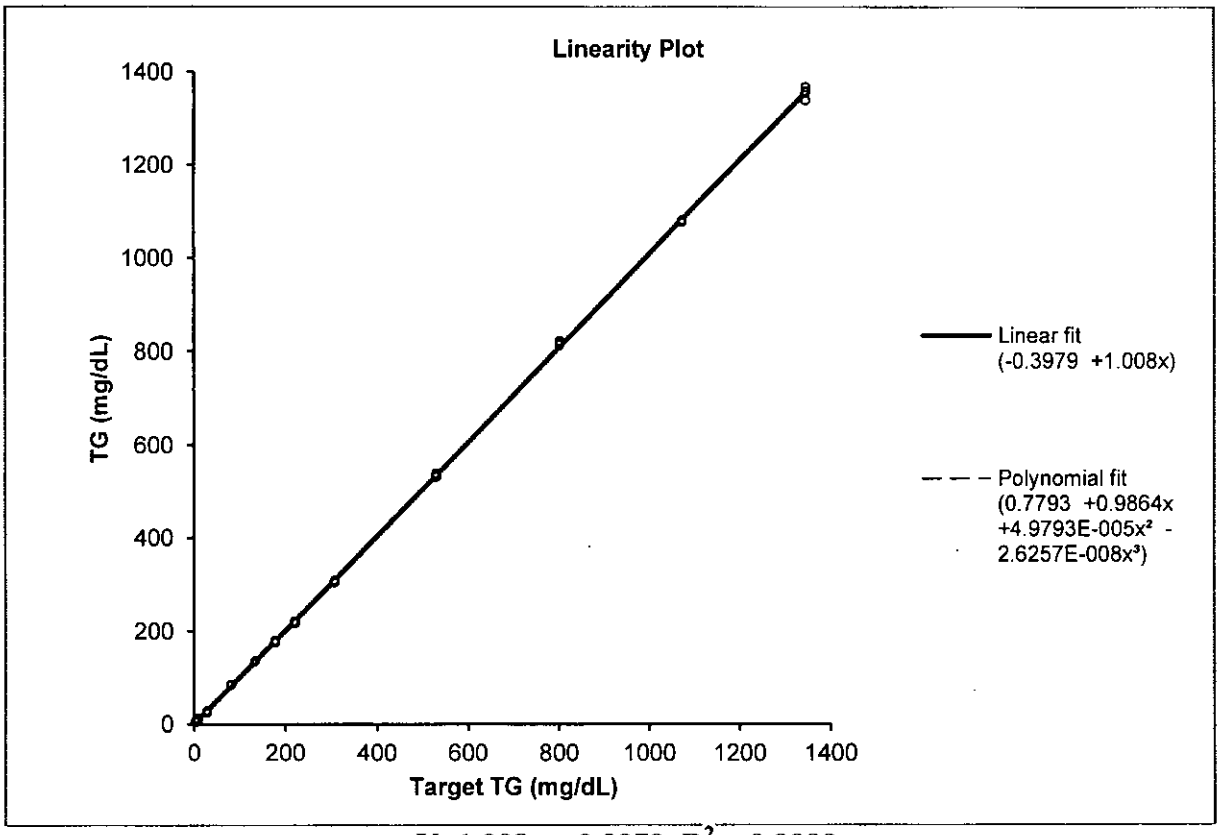
Level	1	2	3	4	5	6	7	8	9
Target value	6.13	21.44	28.19	35.56	42.94	50.31	72.75	110.25	147.75
Observed Mean	5.00	22.50	29.25	36.25	43.25	50.75	81.50	117.25	151.50
% Bias	-	5.0	3.8	1.9	0.7	0.9	12.0	6.3	2.5



$Y=1.0486x - 0.3459$, $R^2 = 0.9961$

Triglycerides Measuring Range: 5-1100 mg/dL

Level	1	2	3	4	5	6	7	8	9	10	11	12	13
Target value	3.8	5.1	9.2	29.0	82.5	134.6	178.1	221.5	308.4	531.0	802.6	1074.2	1345.7
Observed average	5.5	6.8	11.0	26.3	84.5	135.0	177.8	219.3	306.0	536.0	816.8	1079.0	1356.3
% Bias	43.1	31.7	19.2	-9.5	2.4	0.3	-0.2	-1.0	-0.8	0.9	1.8	0.5	0.8



$Y=1.008x - 0.3979$, $R^2 = 0.9999$

Reportable Range

The following are the reportable ranges for LDL-P, HDL-C and Triglycerides:

LDL-P	300 – 3500 nmol/L
HDL-C	7 – 140 mg/dL
Triglycerides	5 – 1100 mg/dL

Traceability, Stability, Assigned values (controls, calibrators)

The NMR Reference Standard

The NMR Reference Standard, TMA (Trimethylacetic acid, Sodium salt), is used as the NMR calibrator for the Vantera Clinical Analyzer. TMA is used routinely as a calibrator once daily during instrument startup to establish daily normalization factors. It also serves as a quality assessment tool to ensure quality NMR spectra are produced by the NMR analyzer.

The stability of the TMA calibrator material and storage conditions was evaluated for a period of 18 months across multiple NMR Analyzers. It was stored at room temperature and refrigerated at 4°C, in glass bottles and plastic bottles. TMA samples were evaluated for TMA signal methyl integrals every other month. The quality of the TMA spectra was not affected by the storage conditions during the study. The NMR Reference Standard is stable for 18 months in either glass or plastic bottle regardless of room temperature or refrigerated storage.

Liquichek™ Lipids Control

Liquichek™ Lipids Control material for LDL-P is frozen human serum in two pools, Level 1 and Level 2, prepared and packaged by Bio-Rad Laboratories. To assign values, new lots of Liquicheck™ Lipids Control material are run on 3 qualified Vantera Clinical Analyzers in house for 3 days. Means, Standard Deviations and % CVs are computed and new values are assigned.
The Liquicheck™ Lipids Control material is stable up to 6 months. Change in recovery over this period was estimated to be less than 0-6% for LDL-P.

Interfering Substances

Endogenous substances normally found in blood and exogenous substances (common and prescription drugs) were evaluated for potential interference with the *NMR LipoProfile®* test by LipoScience. Seven endogenous agents and twenty three drugs were screened for potential interfering effects to *NMR LipoProfile* test using concentrations in accordance to CLSI EP7-A2 guidelines.

Endogenous

Potential Interferent	***Test Concentration***
Hemoglobin	0.5 g/dL
Bilirubin, unconj.	342 µmol/L 20 mg/dL
Creatinine	442 µmol/L 5 mg/dL
Urea	42.9 mmol/L 260 mg/dL
Uric acid	1.4 mmol/L 23.5 mg/dL
Protein (albumin)	6 g/dL60g/L
Bilirubin, conj	342 µmol/L 28.9 mg/dL

Exogenous (OTC drugs, etc.)

Potential Interferent	***Test Concentration***	***Potential Interferent***	***Test Concentration***
Acetaminophen	1324 µmol/L	Metformin Hydrochloride	3.62 mmol/L
Acetylsalicylic acid	3.62 mmol/L	Metoprolol tartrate	18.7 µmol/L
Atorvastatin	600 µg Eq/L	Naproxen Sodium	2170 µmol/L
Clopidogrel hydrogensulfate**	95.7 µmol/L	Nicotinic Acid Sodium salt	8.28 mmol/L
Enalaprilat Dihydrate	0.86 µmol/L	Nifedipine	1156 nmol/L
Fenofibrate	125 µmol/L	Pioglitazone hydrochloride	152.7µmol/L
Furosemide	181 µmol/L	Piroxicam	181 µmol/L
Glipizide	4.48 µmol/L	Pravastatin	107.5 µmol/L
Hydralazine hydrochloride	915.4 µmol/L	Salicylic Acid*	1.3 mmol/L
Heparin	3000U/L	Simvastatin	114.7 µmol/L
Ibuprofen Sodium salt	2425 µmol/L		
Isosorbide dinitrate	636 nmol/L		
Menhaden oil (Fish Oil)	2.4 mg/mL		

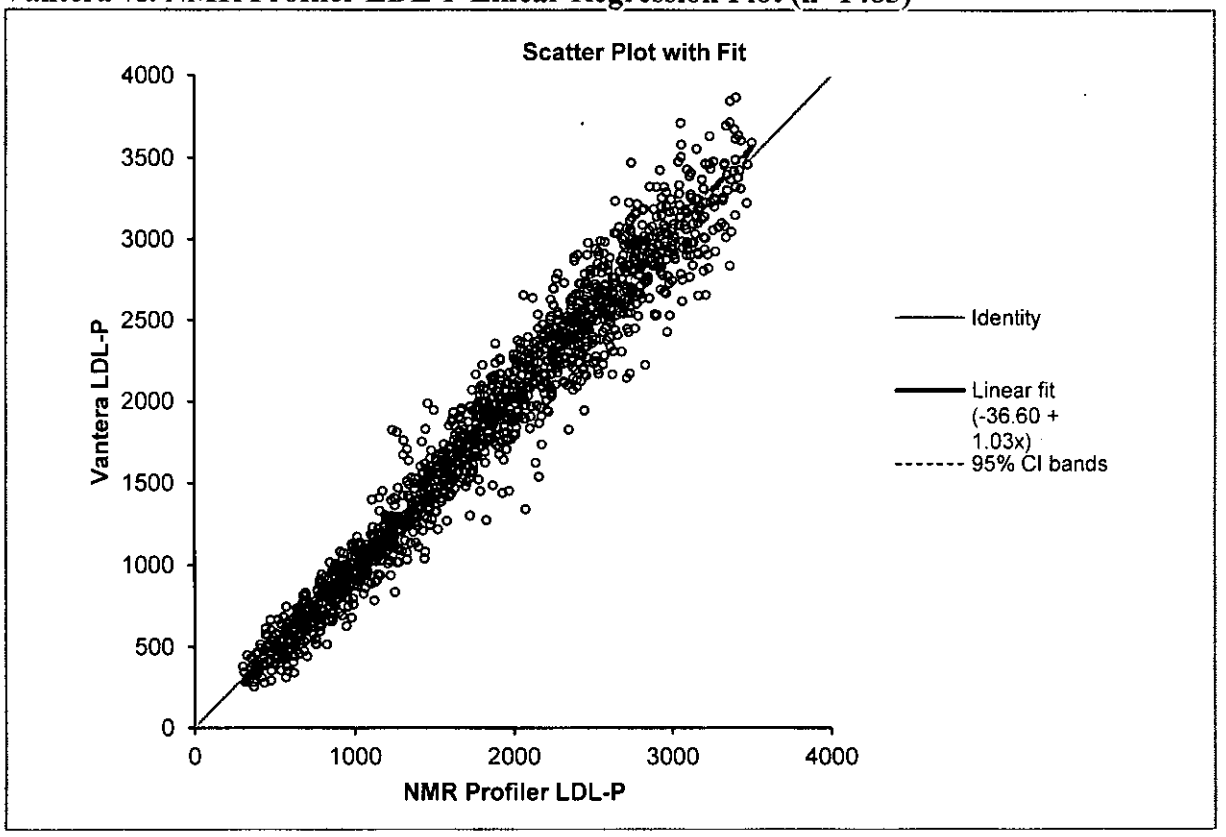
*Salicyclic acid at ≥ 1.3mmol/L was determined to interfere with LDL-P
**Clopidogrel hydrogensulfate at ≥ 95.7 µmol/L was determined to interfere with LDL-P

H. Method Comparison – Non-Clinical:

Method Comparison – LDL-P

Method comparison was evaluated by using serum samples across the reportable range of the *NMR LipoProfile* test for LDL-P on the Vantera Clinical Analyzer. LDL-P concentrations ranged from 303.0 to 3505.0nmol/L.

Vantera vs. NMR Profiler LDL-P Linear Regression Plot (n=1483)

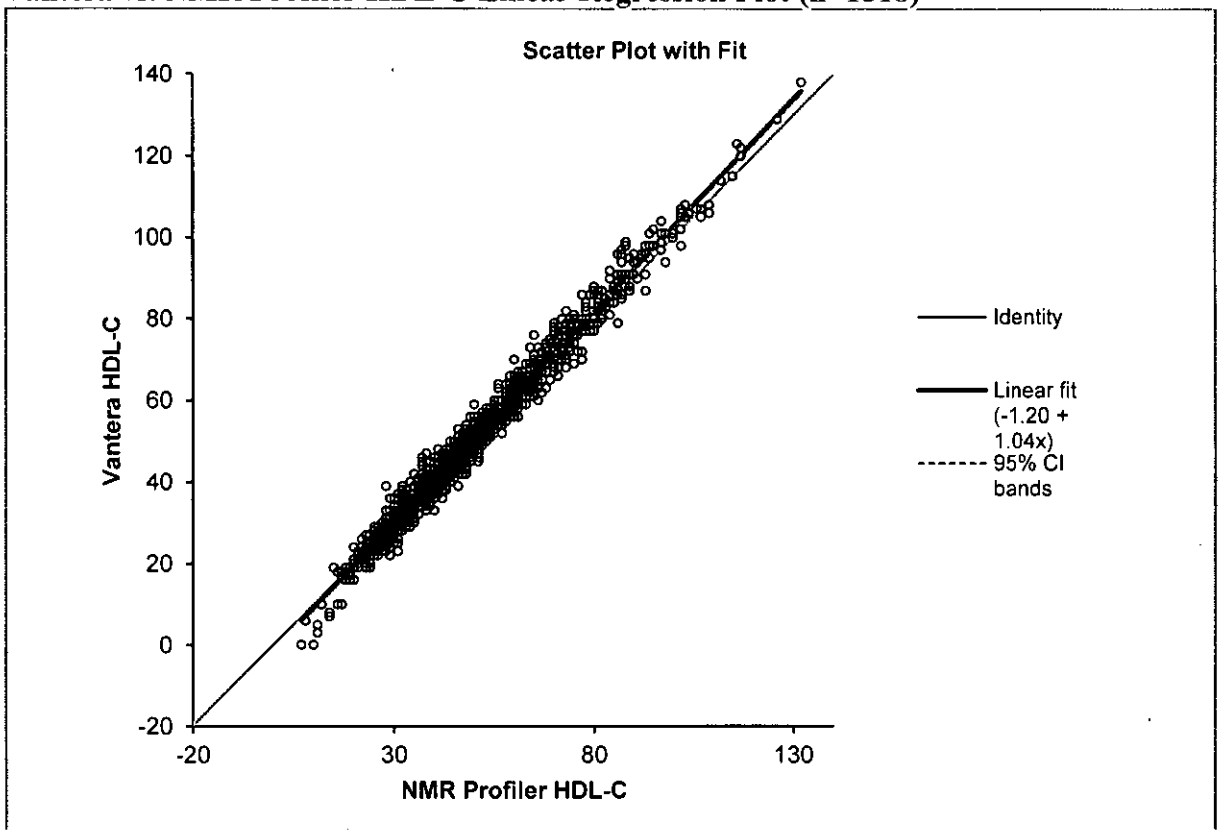


Y=1.03x – 36.60 r=0.978

Method Comparison – HDL-C

Method comparison was evaluated by using serum samples across the reportable range of the *NMR LipoProfile* test for HDL-C on the Vantera Clinical Analyzer. HDL-C concentrations ranged from 7.0 to 132 mg/dL.

Vantera vs. NMR Profiler HDL-C Linear Regression Plot (n=1518)

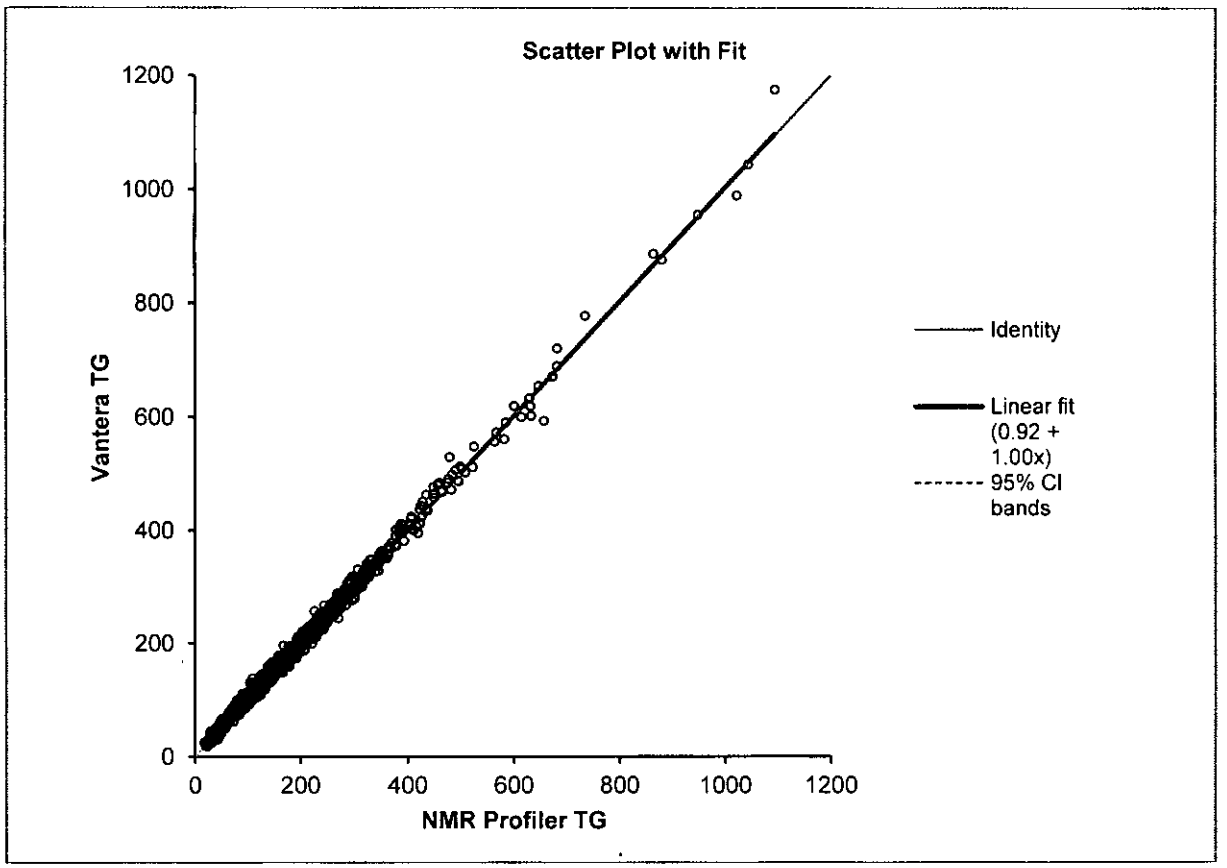


Y= 1.04x – 1.20 r=0.989

Method comparison Triglycerides

Method comparison was evaluated by using serum samples across the reportable range of the *NMR LipoProfile* test for Triglycerides on the Vantera Clinical Analyzer. Triglyceride concentrations ranged from 18.0 to 1095.0 mg/dL.

Vantera vs. NMR Profiler TG Linear Regression Plot (n=1520)



Y=1.00x + 0.92 r=0.998

K. Standard/Guidance Documents Referenced (if applicable):

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.

Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems

EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approves Guideline – Second Edition

EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition

EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline

EP14-A2: Evaluation of Matrix Effects: Approved Guideline – Second Edition

C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical

C53-A: Characterization and Qualification of Commutable Reference Materials for Laboratory Medicine; Approved Guideline

IEC 61010-1:2001-2nd Edition: Safety requirements for electrical equipment for measurement, control and laboratory use Part: General requirements

This device has not been tested by the Cholesterol Reference Method Laboratory Network.

M. Clinical Studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

1. Clinical cut-off:

Not Applicable

2. Expected values/Reference range:

In order to determine the distribution of LDL-P levels expected in a representative sampling of the general population, serum samples (n=452) were analyzed from apparently healthy men (n=158) and women (n=294) (ranging from 18 to 84 years). The following table provides the concentrations of LDL-P by percentile in this reference population:

Distribution of LDL-P Observed in a Reference Population

	All (n=452)	Men (n=158)	Women (n=294)	All (n=452)	Men (n=158)	Women (n=294)
Percentile	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-P (nmol/L)	LDL-C (mg/dL)	LDL-C (mg/dL)	LDL-C (mg/dL)
5	539	528	542	63	62	65
10	643	713	638	75	76	75
20	784	883	749	84	90	83
30	909	1004	863	94	100	91
40	1009	1087	970	102	107	98
50	1127	1241	1070	109	113	109
60	1248	1366	1202	118	128	115
70	1396	1505	1322	129	137	124
80	1572	1676	1482	140	147	136
90	1894	1941	1818	157	161	151
95	2047	2169	1986	169	171	169

Based on the recommendations from a National Lipids Association expert panel, suggested reference values are provided in Table 2. The recommendation by the NLA has not been validated by a clinical study. Each laboratory should verify the validity of these reference values for the population it serves.

Recommended LDL-P Reference Values

LDL-P, nmol/L			
Classification			
	Intermediate		
Low / Normal	*Moderate*	*Borderline High*	*High*
< 1000	1000-1299	1300-1599	≥ 1600

HDL Cholesterol and Triglycerides
The following reference values for patient classification have been recommended by the NCEP and Adult Treatment Panel III Guidelines for HDL cholesterol and triglycerides for the assessment and management of CVD risk. Each laboratory should verify the validity of these reference values for the population it serves.

HDL Cholesterol, mg/dL	
Classification	
Low	*High*
< 40	≥ 60

Triglycerides, mg/dL			
Classification			
Normal	*Borderline High*	*High*	*Very High*
< 150	150-199	200-499	≥ 500

O. System Description:

1. Modes of Operation:

   The Vantera Clinical Analyzer is a 400 MHz proton nuclear magnetic resonance spectrometer.

2. Software:

   The FDA has reviewed the applicant's Hazard Analysis and software development process for this line of product type:

   Yes _____ No_____

3. Specimen Identification:

   Bar code of source tube

4. Specimen Sampling and Handling:

   The processing of specimens on the Vantera Clinical Analyzer starts with their placement on the system. The user places serum or plasma specimen tubes in racks, and then places the racks on the system. After reading the bar code on a specimen tube, the system schedules the test or tests to be performed. The specimen is then aliquoted by the Metering Arm and is transferred to a dilution cup. Samples are prepared by diluting 2-fold (1:1) with specimen Diluent 1 performed by the Metering Arm assembly.

5. Calibration:

   The instrument is calibrated with an aqueous solution of Trimethyl Acetate (TMA) as a disodium salt (15.0 mM) containing Na_2EDTA (5.0 mM), $CaCl_2$ (3.0 mM), KCl (120mM), D_2O 10% v/v.

6. Quality Control:

   It is recommended that two levels of quality control materials are tested in the same manner as patient samples, before or during patient sample processing for each analyte being tested. To verify system performance, analyze control materials:

- After calibration
- According to federal, state or local regulations or at least once every day when patient testing is being performed.

Refer to the Liquichek™ Lipids Controls LDL-P value assignment card for LDL-P Target Ranges. It is recommended that each laboratory establish its own mean and acceptance range for each new lot of controls. Patient results should not be reported if the Quality Control values are not within the expected range.

Real-time quality control data indicate that stability for BioRad Liquichek Lipids controls is at least 6 months. A stability study is currently ongoing to extend the dating for the Bio-Rad Liquichek Lipids Controls.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In the "Performance Characteristics" Section above:

Not Applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

LipoScience, Inc.
c/o Suzette Warner
2500 Sumner Boulevard
Raleigh, NC 27616

AUG 30 2012

Re: k113830
Trade Name: Vantera® Clinical Analyzer; NMR LipoProfile® test on Vantera Clinical Analyzer
Regulation Number: 21 CFR §862.2570
Regulation Name: Instrumentation for clinical multiplex test systems
Regulatory Class: Class II
Product Codes: NSU, MRR, LBS, CDT
Dated: July 27, 2012
Received: July 30, 2012

Dear Ms. Warner:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance...

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K113830

Device Name: Vantera® Clinical Analyzer

Indications for Use:

The Vantera® Clinical Analyzer is an automated laboratory test analyzer which measures the 400 MHz proton nuclear magnetic resonance (NMR) spectrum of clinical samples to produce signal amplitudes, converting these signal amplitudes to analyte concentration. The device includes a 400 MHz NMR spectrometer and software to analyze digitized spectral data. This instrumentation is intended to be used with NMR based assays to detect multiple analytes from clinical samples.

Prescription Use X And/Or Over the Counter Use ____
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K113830

Indication for Use

510(k) Number (if known): K113830

Device Name: NMR LipoProfile® test on Vantera® Clinical Analyzer

Indications for Use:

The *NMR LipoProfile®* test, when used with the Vantera® Clinical Analyzer, an automated NMR spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in human serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of HDL-C and triglycerides are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease.

Prescription Use __X__ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K113830